REMARKS

The following is a written record of the substance of the July 9, 2001 interview as recounted by Applicants' attorney and representative.[2]

Should he find any points in the account below to be inaccurate or insufficient, the Examiner is invited to correct or provide any information so that the understanding of the participants is not misplaced.

A brief discussion was held among the participants at the beginning of the interview concerning the claim amendments which were effected by Applicants' January 18, 2001 Amendment Under 37 C.F.R. §1.116. Applicants' attorney explained that these amendments were made in a good faith belief that they would be implementing the discussions from the previous interview held on August 24, 2000.[3] Those discussions included adding "probe" language to the then pending claims in order to distinguish more clearly Applicants' invention from the prior art, such as Halloran et al. and Miller et al. The Examiner responded briefly to the claim amendments, indicating that he would maintain the non-entry of those amendments. Thus, the claims pending prior to Applicants' January 18, 2001 Amendment constituted the claims now pending for purposes of examination and appeal to the Patent Board of Appeals & Interferences.

It was generally agreed by the Examiner, Applicants' representative and their attorney that the compositions embraced by the pending claims defined nucleic acid hybridization probes.

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[2] Both Mr. DeLucia and Applicants' attorney appreciate that Examiner Houtteman took the time and effort to meet with them to discuss the several outstanding issues in this application.

[3] In the August 24, 2000 Interview Summary, the Examiner wrote

> "Applicant's position is the prior art does not attach labels but merely fragments of proteins and that the resulting product can not be used as a probe."

Applicants' claimed embodiment for attaching the non-radioactive detectable Sig moiety to the phosphorus atom of the phosphate moiety (PM) was also discussed in regard to the written description rejection. Applicants' attorney and their representative explained that the specification disclosed nine separate instances where the non-radioactive detectable Sig moiety is described as being attached to the phosphate moiety (PM). They further explained that originally filed claim 141 showed Sig attached to the oxygen atom of PM and that Example V (page 57 in the specification) showed that a labeled protein (polybiotinylated poly-L -lysine) could be attached to the phosphorus atom or to the oxygen atom of PM using the carbodiimide coupling procedure described by Halloran and Parker (1966). Applicants' attorney indicated that these disclosures were clear evidence that Applicants were in possession of their claimed subject matter in which the non-radioactive detectable Sig moiety was attached to the phosphorus atom of PM. The Examiner indicated that he would maintain the written description rejection against the claims in which Sig is attached to the phosphorus atom of the phosphate moiety (PM).[4]

In closing the discussion on written description and the attachment of Sig to the phosphorus atom in the phosphate moiety, Applicants' attorney referred to the statements in Dr. Agris's Declaration concerning "essential or critical features" (paragraph 27 C, page 26 in the Declaration). Applicants' attorney reiterated the point made by Dr. Agris that the specification did not require that Sig be attached to the oxygen atom in the phosphate moiety, and he cited the nine separate instances (Sig attached to PM), originally filed claim 141 and Example V

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[4] Although not specifically identified at the July 9, 2001 interview, claims 454, 457, 463, 491, 514, 520 and 548 are embodiments in which Sig is attached to the phosphorus atom of the phosphate moiety (PM).

(specification, page 57). Applicants' attorney further explained that he felt that this point may have been mis-interpreted by the Examiner in the May 30, 2001 Advisory Action where it is stated that "atoms present in a chemical compound must be considered a 'critical element' of a claim to a chemical compound." Applicants' attorney explained that Dr. Agris was referring to a legal doctrine called the "omitted element" which was laid down in a series of three cases (Gentry Gallery Furniture, Microsoft/Reiffin and Tronzo). According to Applicants' attorney, the doctrine basically says that if you always describe an element as "A," you cannot suddenly claim it as "B." He further explained that in no way was Dr. Agris saying that atoms are "not critical" to a chemical compound; rather, she was invoking the "omitted element" doctrine of those three cases to make the point that in the specification the oxygen atom is not the only site of attachment of Sig to the phosphate moiety.

Also discussed at the interview was the written description issue directed to the chemical linkages of Sig to the phosphate moiety (PM). Applicants' attorney explained that the first fifty-two pages of the specification contained the patent disclosure of Ward et al. which is identified as U.S. Patent Application Serial No. 255,223. Applicants' attorney also explained that Ward's patent disclosure covered nucleic acids non-radioactively labeled in the non-disruptive base positions, notably the 8-position of purines, the 7-position of deazapurines and the 5-position of pyrimidines. The present invention, it was explained, departed from Ward's patent disclosure in its focus on the non-radioactive labeling of nucleic acids in the disruptive or semi-disruptive positions of the phosphate moiety (PM). Applicants' attorney indicated that Ward's patent disclosure was initially deleted in the June 7, 1995 Preliminary Amendment in a good faith belief that it would improve the readability of the present specification because Ward's patent disclosure had

already been incorporated by reference. Later, after further reflection, Applicants' attorney decided to re-insert Ward's patent disclosure in the June 22, 2000 Second Supplemental Amendment, this time believing that its re-insertion would improve the readability of the present application by providing information to future readers without necessitating resort to another patent disclosure.

Having outlined the above history with respect to Ward's patent disclosure, Applicants' attorney went on to explain that Ward's chemical linkages are described in the present specification as being applicable to the present invention and claims. The Examiner was referred to the bridging paragraph on pages 97-98 in the specification.[5] This bridging paragraph reads as follows:

> The Sig component of the nucleotides in accordance with this invention and the nucleotides and polynucleotides incorporating the nucleotides of this invention containing the Sig component are equivalent to and useful for the same purposes as the nucleotides described in the above-identified U.S. patent application Serial No. 255,223. More specifically, the chemical moiety A described in U.S. patent application Serial No. 255,223 is functionally the equivalent of the Sig component or chemical moiety of the special nucleotides of this invention. Accordingly, ***the Sig component or chemical moiety of nucleotides of this invention can be directly covalently attached to the P, S or B moieties or attached thereto via a chemical linkage or linkage arm as described in U.S. patent application Ser. No. 255,223, as indicated by the dotted line connecting B and A of the nucleotides of U.S. Serial No. 255,223. The various linker arms or linkages identified in U.S. Ser. No. 255,223 are applicable to and useful in the preparation of the special nucleotides of this invention***.
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> [emphasis added above]

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[5] Applicants' attorney also pointed out that on page 24 in her Declaration that was submitted with the January 18, 2001 Amendment, Dr. Cheryl H. Agris cited the same bridging paragraph from pages 97 and 98 of Applicants' specification.

The Examiner indicated that the disclosure above does not meet the requirements for written description because although it may describe the chemical linkages, the disclosure does not place the chemical linkages in Applicants' possession with respect to the phosphate moiety. Applicants' representative responded that other issues might be raised with regard to the disclosure in question, but that the language in the bridging paragraph (pages 97-98) reasonably conveys that Applicants were in possession of the claimed chemical linkages for attaching Sig to the phosphate moiety.

The participants also discussed the chemical linkages in the context of the enablement rejection. The Examiner reiterated his position that the disclosure did not enable the attachment of the various chemical linkages disclosed in the specification to the phosphate moiety. However, the Examiner did not identify which if any of the chemical linkages or reaction conditions posed an enablement synthetic hurdle which are beyond the level of the ordinarily skilled organic chemist. Indeed, Applicants' representative responded by referring to the Declaration of Dr. Dean L. Engelhardt, one of the named inventors, who submitted almost a dozen papers which show modifications (but no non-radioactive detectable labels) to the oxygen or to the phosphorus atom in the phosphate moiety. All of the papers bore pre-filing publication dates. Thus, the enablement rejection in Applicants' view is overcome by the submissions of record.

The obviousness rejection based on two separate publications, Halloran and Parker, and Miller et al., was also discussed. Applicants' attorney explained that neither Halloran nor Miller disclosed the instantly claimed non-radioactively labeled detectable nucleic acid hybridization probes in their papers. In the case of Halloran and Parker, the authors disclosed a nucleotide-protein conjugate in which carbodiimide was used to couple an unlabeled protein with a mononucleotide or a

polynucleotide. Applicants' attorney further explained that Halloran's conjugates were not nucleic acid hybridization probes in any sense because first, no label in the form of a chemical modification was ever made to the protein or nucleic acid. Second, no hybridization was ever undertaken; instead, Halloran and Parker merely attempted to make a conjugate of a protein and a nucleic acid to stimulate antibody formation for the purpose of studying RNA and DNA structure. Finally, no signal was ever generated from Halloran's conjugates either before or after hybridization; instead, the authors merely localized -- using separate protein and nucleic acid stains -- the protein and DNA following electrophoresis.

In the case of Miller et al., Applicants' attorney explained that because methylphosponates increased resistance to cleavage by nucleases, their disclosed radioactively labeled oligodeoxyribonucleoside methylphosphonates were used to study uptake and biological effects in mammalian and bacterial cells. Unlike the non-radioactively labeled nucleic acid compositions of the present invention, Miller's oligodeoxynucleoside methylphosphonates were radioactively labeled with tritium (^3H), and thus, those compositions of Miller were outside of the non-radioactive detectable Sig moiety labeled nucleic acid probe compositions of Applicants' invention.

Applicants' attorney also pointed out that the second obviousness rejection, Gohlke et al. in view of Sodja and Davidson, was not discussed in the May 30, 2001 Advisory Action; nor was the declaration by one of the authors, Dr. Ann Sodja, mentioned in the Advisory Action. Dr. Sodja's Declaration was submitted with Applicants' January 18, 2001 Amendment in support of the non-obviousness of the present invention. Applicants' attorney explained that the periodate oxidation chemistry disclosed in Dr. Sodja's cited 1978 paper could only be used for RNA and its terminally free 2', 3' OH ends. It was further explained by

Applicants' attorney that the claims drawn to RNA contained a proviso that specifically excluded chemical linkages in which a 3' terminal ribonucleotide was cleaved and used to attach Sig to an oligo- or polyribonucleotide.[6] In response to the Examiner's inquiry, Applicants' attorney indicated that independent claims 511 and 539 were drawn to oligo- or polyribonucleotides having such proviso language. After considering Dr. Sodja's Declaration and the statements by Applicants' attorney, the Examiner indicated that he would remove the second obviousness rejection which was set forth in Paragraph 5 in the July 18, 2000 Office Action. See the Interview Summary attached to this Communication as Exhibit A.

In response to a question posed by their attorney at the end of the interview, the Examiner indicated that Applicants could submit a paper to summarize the substance of the interview.[7] The Examiner also indicated that he might re-consider the application of the 112 issues against the remaining obviousness rejection.

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[6] The proviso language in question recites:

"provided that when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not a cleaved 3' terminal ribonucleotide previously attached to said oligo- or polyribonucleotide."

[7] Applicants' attorney has arranged for a courtesy copy of this Communication to be hand delivered to Examiner Houtteman, Group Art Unit 1656.

SUMMARY AND CONCLUSIONS

As discussed at the July 9, 2001 interview, the purpose of this Communication is to provide a separate record of the substance of the interview.

If a telephone conversation would further the prosecution of the present application, Applicants' undersigned attorney requests that he be contacted at the number provided below.

Respectfully submitted,

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